REMARKS

Applicant respectfully requests reconsideration and allowance of all pending claims.

I. Status of the Claims

Upon entry of this Amendment A, claims 1-23 remain pending in this application, while claims 24-49 have been canceled.

Claims 1, 3-5 and 9 have been amended herein to more particularly claim certain embodiments. Support for the amendments to claims 1 and 9 may be found in claims 3 and 5 as originally filed, as well as in, for example, paragraphs [00010] and [00015] of the application. Support for the amendments to claims 3-5 may be found, for example, in the following paragraph of the application:

Claim 3: paragraph [00015];

Claim 4: paragraphs [0008-9]; and,

Claim 5: paragraphs [00010-15].

II. Restriction

Claims 24-49 have been canceled in response to the Restriction Requirement dated March 29, 2007, these claims being drawn to non-elected inventions. As previously noted, Applicant respectfully reserves the right to pursue the subject matter of these canceled claims in one or more divisional applications.

III. Objection

The objection raised by the Office to the oath has been noted. A new oath in compliance with 37 C.F.R. 1.67(a), as well as M.P.E.P. 602.01 and 602.02, is being filed concurrently with this Amendment A. The new oath includes a reference to PCT application serial number PCT/US04/033268, from which the present application claims priority.

Withdrawal of the present objection is therefore respectfully requested.

IV. 35 U.S.C. 112 Rejection

Applicant respectfully requests reconsideration of the rejection of claim 6 under 35 U.S.C. 112, second paragraph for lacking insufficient antecedent basis for the phrase "ascorbic acid."

Claim 6 of the present application, as originally filed and as currently pending, reads as follows:

> 6. The methylphenidate solution according to claim 1, wherein the at least one **organic acid** is selected from the group consisting of acetic acid, **ascorbic acid**, citric acid, fumaric acid, malic acid, succinic acid, tartaric acid and mixtures thereof. (Emphasis added)

Applicant submits that one of ordinary skill in the art would recognize that "ascorbic acid" is an organic acid. In fact, it is clearly identified as such in paragraph [00016] of the present application.

In view of the foregoing, proper antecedent basis for "ascorbic acid" is present in claim 6. Withdrawal of this rejection is therefore requested.

V. 35 U.S.C. 103(a) Rejection

Reconsideration is requested of the rejection of claims 1-23 under 35 U.S.C. §103 as being obvious in view of the combination of Midha et al. (U.S. Patent No. 6,127,385) and Epstein et al. (U.S. Patent Publication No. 2002/0103162).

A. The Claimed Subject Matter

The present application is directed to a methylphenidate solution (e.g., a solution of the free base or a pharmaceutically acceptable salt thereof) that has improved chemical stability, and therefore improved shelf life as well. (See, e.g., paragraph [0001].) As noted in the present application, Applicant has discovered that by preparing a solution of methylphenidate using a **solvent system** comprising a combination of water and a non-aqueous solvent, and in particular a solvent system comprising **less than about 50% water** (or alternatively **greater than about 50% of the non-aqueous solvent**), the chemical stability, and therefore the shelf life, of the solution is improved. (See, e.g., paragraph [0008] and [00010].) As illustrated in Applicant's working examples, such solutions have been observed to have a projected shelf life of at least two years. (See, e.g., paragraph [00021] therein.)

More particularly, the claims of the present application are directed to the following:

> Claim 1, from which claims 2-8 depend, is directed to a methylphenidate solution comprising, in relevant part, methylphenidate and at least one pharmaceutically acceptable organic acid dissolved in a **solvent system**, the solvent system **comprising between about 10% and about 45% water** and **at least about 50%** of at least one **non-aqueous solvent**.
>
> Claim 9, from which claims 10-13 depend, is directed to a methylphenidate HCl solution comprising, in relevant part,

methylphenidate HCl and at least one organic acid dissolved in a **solvent system**, the solvent system comprising **less than about 50% water**, between **about 30% and about 70%** of at least one **polyol** solvent, and between **about 10% and about 70%** of at least one **glycol** solvent.

Claim 14, from which claims 15-18 depend, is directed to a methylphenidate HCl solution comprising, in relevant part, methylphenidate HCl and at least one organic acid dissolved in a **solvent system**, the solvent system comprising between **about 10% and about 45% water**, between **about 40% and about 60%** of at least one **polyol** solvent, and between **about 10% and about 30%** of at least one **glycol** solvent.

Claim 19, from which claims 20-23 depend, is directed to a methylphenidate HCl solution comprising, in relevant part, methylphenidate HCl and at least one organic acid dissolved in a **solvent system**, the solvent system comprising between **about 30% and about 40% water**, between **about 45% and about 55%** of at least one **polyol** solvent, and between **about 10% and about 20%** of at least one **glycol** solvent.

B. The Cited Art

Midha et al. disclose a method of treating depression in a patient by oral or non-oral administration of the active 1-threo-methylphenidate, which may be in the form of the free base or a pharmaceutically acceptable salt. (See, e.g., column 1, lines 5-8, and column 2, lines 36-38). Although they make a general reference to a solution containing the active, ascorbic acid, and an aqueous or non-aqueous solvent (see, e.g., column 4, lines 59-63), they **fail to disclose or suggest** a solution comprising the active in a **solvent system** that in turn comprises both water and a non-aqueous solvent, **wherein the concentration of water therein is less than about 50%**. In fact, they do not make any specific reference at all to the concentration of water, or the concentration of the non-aqueous solvent, in a solution that contains both in combination with the active. Applicant respectfully submits this is because Midha et al. are simply not concerned about the stability or shelf life of such a solution; evidence of this may be found in the fact that they do not even reference these as factors to be considered when preparing such a solution.

Epstein et al. disclose methods and compositions for enhancing long-term memory function and/or performance. (See, e.g., paragraph [0006].) Although they make a general reference to the preparation of a solution of a methylphenidate compound using, among other things, water, a polyol or a mixture thereof (see, e.g., paragraph [0250]) as a solvent, like Midha et al., they

also fail to disclose or suggest a solution comprising the active in a **solvent system** that in turn comprises both water and a non-aqueous solvent, **wherein the concentration of water therein is less than about 50%.** In fact, they do not make any specific reference at all to the concentration of water, or the concentration of the non-aqueous solvent, in a solution that contains both in combination with the active. Applicant respectfully submits this is because Epstein et al., like Midha et al, are simply not concerned about the stability of shelf life of such a solution; evidence of this may be found in the fact that they too fail to even reference these as factors to be considered when preparing such a solution.

C. The Claimed Subject Matter is Not Obvious

As set forth in M.P.E.P. §2143, in order for the Office to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) the prior art references, when combined, must teach each and every element of the claim; (2) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine or modify the references; and (3) there must be some reasonable expectation of success. Applicant respectfully submits the Office has failed to establish a *prima facie* case of obviousness, because (i) each and every element of the claims have not been disclosed or suggested, and/or (ii) motivation is simply not provided to prepare the claimed methylphenidate solution.

Applicant submits that Midha et al. and Epstein et al., both alone and in combination, fail to disclose a solution comprising, among other things, methylphenidate, or methylphenidate HCl, and a solvent system that has a water concentration of less than 50%. More specifically, the combination of Midha et al. and Epstein et al. fail to disclose a solution comprising such a solvent system, wherein:

> (i) the water concentration is between about 10% and about 45% and the non-aqueous solvent concentration is at least about 50% (Claim 1);
>
> (ii) the water concentration is less than about 50%, the polyol concentration is between about 30% and about 70%, and the glycol concentration is between about 10% and about 70% (Claim 9);
>
> (iii) the water concentration is between about 10% and about 45%, the polyol concentration is between about 40% and about 60%, and the glycol concentration is between about 10% and about 30% (Claim 14); or,
>
> (iv) the wafer concentration is between about 30% and about 40%, the polyol concentration is between about 45% and

about 55%, and the glycol concentration is between about 10% and about 20% (Claim 19).

Notably, both Midha et al. and Epstein et al. **fail to disclose or suggest any specific details** relating to a solution comprising methylphenidate as the active in combination with water and another non-aqueous solvent; that is, neither provide details of the water content or the non-aqueous solvent content in such a solution.

Applicant also submits that there is simply no motivation for one of ordinary skill in the art to modify the disclosure of Midha et al. and Epstein et al. in order to prepare a solution comprising a solvent system as recited in any one of claims 1, 9, 14 or 19, because **neither Midha et al. nor Epstein et al. provide any link between the solutions they generally reference and stability or shelf-life thereof.** In fact, as previously noted above, they do not even identify stability or shelf-life as a factor to be considered when preparing such solutions.

Applicant notes the Office's assertion that:

> it is obvious to vary and/or optimize the amounts . . . of aqueous and non-aqueous solvents . . ., according to the **guidance** provided by Midha et al. and Epstein et al. to provide a composition having the desired properties such as the desired concentrations and percentages of each component to formulate an effective methylphenidate solution **for administration.** (See the present Office action at page 4, first full paragraph. Emphasis added.)

However, Applicant respectfully submits that providing guidance for preparation a solution of methylphenidate for "administration" is not the issue here. Rather, the issue is providing motivation to prepare a solution having improved stability and shelf life, and thus having the composition as claimed. Applicant respectfully submits Midha et al. and Epstein et al. provide no such motivation.

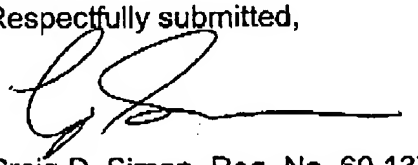
In view of the foregoing, Applicants respectfully submit that the Office has failed to meet its burden in establishing a *prima facie* case of obviousness here, because either (i) each and every element of the claimed solution has not been disclosed or suggested by the combination of Midha et al. and Epstein et al., and/or (ii) motivation is simply not provided by the combination of Midha et al. and Epstein et al. to prepare a solution as claimed. Accordingly, reconsideration of the rejection of claim 1-23 is respectfully requested.

CONCLUSION

In view of the foregoing, Applicant respectfully requests favorable reconsideration and allowance of all pending claims.

Applicant does not believe that a fee is due in connection with the submission of this Amendment A. If, however, the Commissioner determines that a fee is due (either for the submission of Amendment A, or the Declaration being submitted concurrently herewith), authorization is hereby given to charge Deposit Account No. 13-1160.

Respectfully submitted,



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